REMARKS

Pending in this Application are Claims 1, 3, 5, 7, 13 – 15, 17, and 23 – 25.

Applicants have amended Claims 1 and 13 in order to clarify that the mixture of growth factor protein and extracellular matrix degrading protease enzyme comprises at least a biologically active fragment of growth factor protein. Support for this amendment can be found in the Specification at Page 17, lines 11 – 27 and Page 20, lines 9 – 10.

I. Rejections Under 35 U.S.C. §103(a)

Claims 1, 3, 5, 7, 13 – 15, 17, and 23 – 25 stand rejected under 35 U.S.C. §103(a) as being unpatentable over European Patent No. 307847 ("EP 307847"), U.S. Patent No. 4,996,050 ("U.S. '050"), or International Patent Application No. WO 82/03772 ("WO 82/03772"), in view of European Patent No. 619370 ("EP 619370"), U.S. patent No. 5,589,451 ("U.S. '451"), U.S. Patent No. 5,814,605 (U.S. '605"), International Patent Application No. WO 97/13857 ("WO 97/13857"), or International Patent Application No. WO 98/16243 ("WO 98/16243"). The Examiner has asserted that the claims are unpatentable because the combination of a growth factor protein and a protease enzyme is obvious. Specifically, the Examiner states that "[i]f the ingredients are known individually in the art to be used for the same purpose, then to combine them for the same purpose is also obvious." *See* Advisory Action dated August 12, 2004. The Examiner also asserts that combining a growth factor protein and a protease enzyme is obvious because "[n]ot all proteases act on all proteins, i.e. the growth factor." *See* Advisory Action dated December 6, 2004.

There is no basis for concluding that an invention would have been obvious solely because it is a combination of elements that were known in the art at the time of the invention. *See Smiths Industries Medical Systems Inc. v. Vital Signs Inc.*, 183 F.3d 1347, 51 U.S.P.Q.2d 1415, 1420 (Fed. Cir. 1999). A person of skill in the art would expect that mixing the two components would produce a mixture of an inactive, degraded protein and an active protease

enzyme. Such a mixture would be no more useful than a protease enzyme alone. Even if, as the Examiner asserts, different proteases act on different proteins, there is no certainty in the art as to which proteins will retain biological activity when mixed with a protease enzyme, nor whether such a mixture will retain any usefulness at all. The current claims pertain to a mixture of a protein and a protease enzyme which contains at least a biologically active fragment of protein, and which produces unexpected results, or a synergistic utility that is greater than the use of a protease enzyme or a protein alone. *See* Specification at Page 19, lines 13 – 27. This useful mixture of components is not obvious.

Despite the fact that the two elements individually are used for the same purpose, no one of skill in the art would expect that the combination of two incompatible elements would produce a useful result. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the **prior art also suggests the desirability of the combination**. *See In re Mills*, 916 F.2d 680, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990). Nowhere in the prior art is there a suggestion of the desirability of combining a protein with an enzyme that destroys proteins to produce a useful composition. **Even if growth factor proteins and protease enzymes were known in the art, common sense indicated that combining the two would be unproductive, or at least less productive than either element alone.**

Where all elements of an invention were known in the prior art, but not utilized together, if the combination produces unexpected results different from the prior art, the invention may be patentable, particularly where the prior art indicates that the procedure utilized by the patent will be unproductive. *See Milgo Electronics Corp. v. United Telecommunications, Inc.*, 189 U.S.P.Q. 160, 168 (Kan. 1976); *see also W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 U.S.P.Q. 303, 312 (Fed. Cir. 1983); *In re Hedges*, 783 F.2d 1038, 228 U.S.P.Q. 685, 687 (Fed. Cir. 1986) (noting that proceeding contrary to the accepted wisdom of the prior art is strong evidence of nonobviousness). The claimed mixture produces unexpected results different from the prior art because the mixture of a protease enzyme and a protein would be expected to demonstrate a lack of or minimal activity, compared to either component acting alone. A combination of the two components, which might result in any variation of degradation and

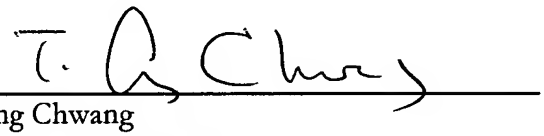
antagonism, would not be expected to produce a biologically active fragment of protein and a synergistic effect that is greater than the use of either component alone.

II. Conclusion

For the reasons stated above, Applicants respectfully submit that Claims 1, 3, 5, 7, 13 – 15, 17, and 23 – 25 are patentable.

If the Examiner has any other matters which pertain to this Application, the Examiner is encouraged to contact the undersigned to resolve these matters by Examiner's Amendment where possible.

Respectfully submitted,



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